Weekly Journal Scan

Atrial fibrosis detected by cardiac magnetic resonance in persistent atrial fibrillation: a useful risk stratifier but not ideal electrophysiological endpoint for catheter ablation

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Comment on ‘Effect of MRI-Guided Fibrosis Ablation vs Conventional Catheter Ablation on Atrial Arrhythmia Recurrence in Patients With Persistent Atrial Fibrillation: The DECAAF II Randomized Clinical Trial’ which was published in the Journal of the American Medical Association, doi:10.1001/jama.2022.8831.

Key Points

• The efficacy of delayed enhancement (DE) MRI-guided fibrosis ablation vs. conventional catheter ablation of atrial fibrillation (DECAAF II) trial, an investigator-initiated, multicentre, randomized clinical trial, with single blinded design, tested the hypothesis that imaging-guided fibrosis ablation in addition to conventional pulmonary veins isolation (PVI) is superior to PVI alone in improving ablation success rates in patients with persistent atrial fibrillation (AF).1

• Before undergoing baseline cardiac magnetic resonance (cMR), 843 patients were randomly assigned in a 1:1 ratio to receive cMR-guided fibrosis ablation plus PVI (Group 1, 421 patients) or conventional PVI alone (Group 2, 422 patients). Patients underwent a first cMR within 30 days before the ablation procedure in order to quantify baseline left atrial fibrosis and a second cMR at 90–180 days to quantify ablation-related scar formation. Randomized treatment was masked to reviewers who assessed cMR quality.

• All patients underwent PVI. After evidence of the pulmonary veins (PV) entrance block, fibrosis-guided ablation was pursued in Group 1. The average age of participants was 62 years and 79% were men. Regarding atrial fibrosis level at baseline, 493 (58%) patients had Stages I and II (≤20% fibrosis) and 350 (42%) had Stages III and IV (>20% fibrosis).

• The primary endpoint of the study was the first confirmed recurrence of atrial arrhythmia (including AF, atrial flutter, or atrial tachycardia) lasting for at least 30 s after the 90-day blanking period. After a follow-up of 12–18 months, the event rate for the primary endpoint did not significantly differ between Group 1 (175/422 patients, 43%) and Group 2 (188/421 patients, 46%) (hazard ratio 0.95; 95% confidence interval, 0.77–1.17; P = 0.63). The primary safety composite outcome was defined by the occurrence of one or more adverse events within 30 days, including stroke or transient ischaemic attack (TIA), PV stenosis, bleeding, heart failure or death, and was higher in Group 1 (9 of 403 patients, 2.2%) than in Group 2 (0 of 428 patients; P = 0.001) largely due to more strokes or TIA (6 vs. 0) in Group 1.

Comment

Atrial fibrillation is an increasingly prevalent arrhythmia associated with significant health burden. Its management improved in the last decades through the growing use of ablative techniques, mostly based on PVI. However, the rate of AF recurrence still remains a significant and challenging issue. In the current prevailing view, AF is believed to be induced by focal triggers arising from the PV in the majority of patients, and consequently an encircling ablation lesion around PV can successfully suppress AF.2 Although PVI remains the most commonly adopted strategy, the approach to ablation varies among centres, with the common goal of protecting the atrium from AF onset and recurrence. A
recent network meta-analysis showed that in patients with persistent AF, a comprehensive ablative strategy including PVI, linear lesion in the left atrium (LA), and ablation of extra-PV sources was associated with reduced risk of recurrent AF compared with PVI alone.9

Left atrium fibrosis, a hallmark of atrial myopathy, seems to play an important role in the pathophysiology of AF and its recurrence. Atrial tissue fibrosis, estimated by DE cMR, was independently associated with the likelihood of recurrent arrhythmia and therefore is currently considered a potential risk stratifier in patients with AF.10 This was supported by the DECAAF study, in which the severity of LA myopathy was classified on the basis of the volumetric percentage of LA DE detected by cMR as Utah Stages (Stage 1 < 10%, Stage 2 ≥ 10 to <20%, Stage 3 ≥ 20 to <30%, Stage 4 ≥ 30%).4

Atrial tissue fibrotic remodelling may indeed contribute to development of AF recurrence,11,12 as there is evidence that fibrosis plays a central role in stabilizing the reentrant drivers that maintain the arrhythmia.7 However, the current results of DECAAF II do not provide evidence that cMR-guided fibrosis ablation improves AF recurrence in the setting of persistent AF.

The most important limitations of this trial are represented by the reproducibility of cMR for DE assessment in LA, and the underlying pathophysiological hypothesis. The location and the extent of atrial fibrosis can be quantitatively assessed by cMR. However, the evaluation of the presence and the extent of DE in LA are limited by atrial thinness as compared for instance to the ventricles, and requires considerable expertise.8 Secondly, the correlation between the histological pattern of atrial fibrosis and the cMR-defined stage remains to be defined. In this regard, in contrast to reactive (interstitial) fibrosis, replacement (reparative) fibrosis substitutes necrotic cardiomyocytes with extracellular matrix tissue and fibroblasts, preserving tissue integrity at the expense of muscle bundle continuity and could be more difficult to reverse than reactive fibrosis. Different forms of fibrosis can co-exist in the atrial tissue, including interstitial and reparative fibrosis, with a variable contribution to AF development.9 Clinical fibrosis imaging by cMR promises to provide useful information to guide AF therapy, but a better understanding of the mechanisms underlying atrial fibrosis seems to be necessary before deciding to target its ablation on the basis of atrial structural remodelling. Another limitation of the study is that two-thirds of total arrhythmia recurrence events were identified by smartphone readings, with consequent limited diagnostic accuracy and low-quality tracings underlying detection.10

With regard to the reduced safety reported with the cMR-guided fibrosis ablation, extensive atrial tissue injury during ablation of atrial fibrotic areas could have affected the function of the LA, with increased risk of clot formation at the ablation site and consequent possible embolic strokes.11 The integration of data from electro-anatomic mapping with cMR or computed tomography images into hybrid maps represents a promising approach, with particular regard to the investigation of ventricular substrate. Based on these findings, cMR could specifically aid in the stratification of AF patients with early stages of atrial fibrosis, but larger studies need to be performed to better identify the vulnerable population with high risk of AF recurrence before catheter ablation.

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Data availability
No new data were generated or analysed in support of this research.

References
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